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(54) Local oral germicide containing hydrogen peroxide

(57) An aqueous oral germicidal composition contains 1—3% by weight of hydrogen peroxide and a flavour which is stable therein the flavour being either methyl salicylate and menthol or cinnamic aldehyde, menthol and clove oil. The preparation may be in the form of a mouthrinse, a paste or a gel. Many optional ingredients may be included such as ethanol, polyhydric alcohols, non-ionic surfactants, fluorides, colour, preservative, sorbitol, surfactants, sodium saccharin, and colour.

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SPECIFICATION

Oral Preparation

The present invention relates to an aqueous oral preparation which contains a peroxygen compound and a flavour which is stable in such a system.

It has long been recognised in the art that hydrogen peroxide and other peroxygen-containing agents are effective in curative and/or prophylactic treatments with respect to caries, dental plaque, gingivitis, periodontitis, mouth odour, tooth stains, recurrent aphthous ulcers, denture irritations, orthodontic appliance lesions, postextraction and postperiodontal surgery, traumatic oral lesions and mucosal infections, herpetic stomatitis and the like. Peroxide-containing agents in the oral cavity exert a chemomechanical action generating thousands of tiny oxygen bubbles produced by interaction with tissue and salivary enzymes. The swishing action of a mouthrinse enhances this inherent chemomechanical action. Such action has been recommended for delivery of other agents into infected gingival crevices. Peroxide mouthrinses and other oral preparations prevent colonisation and multiplication of anaerobic bacteria known to be associated with peridontal disease. Peroxygen-containing gels or pastes are indicated and/or desirable where it is required to selectively treat areas for more than a few seconds, such gels and pastes tending to remain at the site of the application for a time sufficient for the peroxide to manifest its maximum effectiveness.

It is however also known that most peroxy compounds such as magnesium peroxide in such oral compositions, by interaction with other common excipients therein, tend to be unstable in storage, continuously losing the capacity to release active or nascent oxygen over relatively short periods of time, and tend to diminish or destroy the desired function of such excipients. Among such excipients are flavours and colouring agents added to enhance the acceptability of the preparations to those in need of an oral peroxidising treatment. Numerous proposals have been made for solving the afore-mentioned problems, including encapsulating the peroxide compound and/or the peroxide-sensitive excipient, using more stable but more expensive peroxy compounds such as organic peroxides and peroxydiphosphate salts (e.g. the tetrapotassium salt).

The present invention aims to provide oral preparations which will not be subject to one or more of the aforementioned disadvantages and deficiencies. The present invention also aims to provide a foaming oxygenating oral preparation in ready-to-use form having a pleasant flavour and/or colour and enhanced stability in storage. The present invention further aims to provide a mouthrinse having a basis of the readily available, highly effective and economical hydrogen peroxide. The present invention also aims to provide an oral oxygenating preparation in the form of a gel.

According to the present invention there is provided:

an aqueous oral preparation containing, approximately by weight:

A. 1—3% of hydrogen peroxide, and

B. an effective flavouring amount of a flavour selected from the group consisting of:

b1 wintergreen flavour containing methyl salicylate and menthol in a weight ratio of about 3:1 to 5:1, and

b2 a cinnamon flavour composition comprising about 6—9% menthol, 32—38% cinnamic aldehyde and 6—9% clove oil.

The aforementioned component "B" flavours have surprisingly been found to be satisfactorily stable and compatible in the presence of hydrogen peroxide, in contrast to other flavours, e.g. fruity flavours such as orange, lemon and lime, and even minty flavours other than the aforesaid b1 component wintergreen flavour, such as peppermint and spearmint. Effective flavour amounts are as desired, typically ranging from about 0.05 to 1.0%, preferably about 0.1 to 0.5%, by weight of the oral composition.

It is generally desirable, and often preferred to include numerous adjuvants to the basic compositions of the present invention. These include (C) ethanol; (D) polyhydric alcohols such as glycerol and sorbitol; (E) surfactants, especially nonionic surfactants, and of these, those which have been found to have acceptable stability in the aqueous peroxygen environment; (F) a sweetener; (G) anti-caries agent; (H) thickeners; (I) preservatives; (J) colouring agents; and the like.

With references to adjuvant (C), the ethyl alcohol, a convenient amount is 1 to 5% by weight based on the weight of the total composition with 3—10% being a preferred range. The polyhydric alcohol (D) may range from about 1 to 20% by weight, with 3—15% being preferred.

Sorbitol is preferred as the component D polyhydric alcohol since although glycerin is sufficiently compatible with the other components, particularly the hydrogen peroxide, it interferes with at least one common method for analysis of the peroxide content. Component D serves as humectant, carrier (with the ethanol) and viscosity-control agent.

The component E, the surfactant, which is preferably nonionic comprises, in the more preferred embodiments, two general types of surfactants; those known under the Tween and other trade marks and those block polymers available under the Pluronic trade marks. The former (Tween) surfactants are mixtures of C_{10-18} fatty acid esters of sorbitol (and sorbitol anhydrides), consisting predominantly of the monoester, condensed with about 10—30, preferably about 20, moles of ethyleneoxide. The fatty acid (aliphatic hydrocarbyl monocarboxylic acid) may be saturated or unsaturated, e.g. lauric, palmitic, stearic or

oleic acids. Polysorbate 20 (e.g. Tween 20) is especially preferred, commonly referred to as polyoxyethylene (20) sorbitan monolaurate. The Pluronic surfactants are straight chain polymers containing a hydrophobic (water insoluble) polyoxypropylene moiety polyoxyethylenated at both ends with sufficient water-solubilising oxyethylene groups to achieve the desired water-solubility, HLB, (hydrophyliclipophylic balance) and dispersing surfactant activity. The solid F series of Pluronics are preferred in which the molecular weight of the polyoxypropylene moiety ranges from about 950 to 4,000 and constitutes about 20—30% of the molecule (i.e. 80—70% polyoxyethylene in the molecule). Pluronic F108 is especially preferred, in which the said hydrophobic moiety has a molecular weight of about 3250 and constitutes about 20% of the molecule. This surfactant has a molecular weight of about 14,000—16,000.

The surfactant components serve as solubilising, dispersing, emulsifying, wetting and viscosity-control agents and when used in certain combinations, are especially effective to solubilise the flavour.

A particularly useful combination of surfactants is one where at least one surfactant is of the Pluronic type and at least one is of the polysorbate type.

For the aforementioned functions of solubilising, dispersing, emulsifying, wetting and viscosity-control, it is preferred to use from about 0.1% to about 10% by weight of surfactant; a more preferred range is about 0.2% to about 6% and a most preferred range is from about 0.5 to 5%.

Where combinations of Pluronic and Polysorbate surfactants are used they may be employed in weight ratios of from about 20:1 to about 1:10 and preferably from about 10:1 to about 1:5.

As described above the compositions of the present invention may contain other functional agents such as anticaries agents and the like. Fluorine-providing anticaries compounds optionally present in these solutions may be partially or fully water-soluble. They are characterized by their ability to release fluorine-containing ions in water and by substantial freedom from reaction with other compounds of the oral preparation. Among these materials are inorganic fluoride salts, such as soluble alkali metal, alkaline earth metal and heavy metal salts, for example, sodium fluoride, potassium fluoride, ammonium fluoride, calcium fluoride, a copper fluoride such as cuprous fluoride, zinc fluoride, a tin fluoride such as stannic fluoride or stannous chlorofluoride, barium fluoride, sodium fluorosilicate, ammonium fluorosilicate, sodium fluorozirconate, sodium monofluorophosphate, aluminium mono- and di-fluorophosphate, and fluorinated sodium calcium pyrophosphate. Alkali metal and tin fluorides, such as sodium and stannous fluorides, sodium monofluorophosphate (MFP) and mixtures thereof, are preferred.

The amount of the fluorine-providing compound is dependent to some extent upon the type of compound, its solubility, and the type of oral preparation, but it must be a non-toxic amount. An amount of such compound which releases a maximum of about 1% of fluoride ion by weight of the preparation is considered satisfactory. Any suitable minimum amount of such compound may be used, but it is preferable to employ sufficient compound to release about 0.005 to 1%, and preferably about 0.1% of fluoride ion. Typically, especially in the cases of MFP, alkali metal fluorides and stannous fluoride, this component is optionally present in these compositions in an amount of about 0.01 to 2 wt %, preferably about 0.05 to 1 wt %, especially about 0.76 wt %.

A colouring agent is also often desirable for enhanced appearance and acceptability, but should be carefully selected for compatibility with the other named components, particularly the hydrogen peroxide. Green colouring agents for example have been generally found to be unacceptable in this regard. FD & C Blue No. 1 and Red No. 40 have been found to satisfy the requirements of the present invention, employed in effective colouring amounts as desired, typically in concentrations of about 0.0002 to 0.004% by weight in the solution.

A preferred component F sweetener compound is saccharin, especially sodium saccharin, but other known orally acceptable sweetener compounds may be employed, typically in concentrations of about 0.01 to 5 wt % such as xylitol, sodium cyclamate, perillartine, D-tryptophan, aspartame, dihydrochalcones and the like.

One preferred form of the oral compositions of the present invention is as solutions in an aqueous and preferably an aqueous-ethyl alcohol carrier. A typical mode of preparation involves judiciously mixing the selected components for proper solubilization in the carrier medium (e.g. ethanol/polyhydric alcohol/water), any colouring agent and hydrogen peroxide in order being preferably added after any of the other selected components.

As pointed out above one may incorporate into the oral compositions of the present invention any of the conventional preservatives (e.g. in weight amounts of from about 0.0000% to about 5% and preferably about 0.01% to about 1%) which are pharmaceutically acceptable.

Further one may formulate the compositions as gels or pastes utilizing, preferably peroxide-stable thickening and gelling agents. Usable agents include xanthan gum, guar gum, locust gum, carboxylic interpolymers as disclosed in U.S. Patent 2,798,053, Pluronic Polyols particularly of the "10" and "12" Series and of these especially the solid products with a hydrophobe of M.W. of about 3500 to 4000 and with from 30 to 80% hydrophilic polyoxyethylene groups. Examples of such Pluronic compounds are P103, P104, P105, P123, P108 and F127. The most preferred gelling agent is Pluronic F127. The amount of thickener or gelling agent may vary widely. As little as 1 or 2 or 3 or 4 or 5% may suffice for some applications whereas for most gels a most representative range would be 5 to 50% with 10 to 30 preferred and 15 to 25 most preferred.

The pH of the solutions and other pastes and gels of the present invention generally ranges from about

4 to 7, and preferably is about 5. Generally, the pH may be from 6 to 7 when the composition is first prepared and then slowly drop to an equilibrium pH of from about 4 to about 6.

The invention may be put into practice in various ways and a number of specific embodiments will be described to illustrate the invention with reference to the accompanying examples.

All amounts and proportions referred to herein and in the appended claims are by weight unless otherwise indicated.

Typically, in preparing these exemplified formulations, the flavour is first added to the carrier liquid, e.g. ethanol, with agitation. The component E, the surfactants, where used, are then slowly sprinkled in with constant stirring, after which sufficient water is added slowly with stirring for about ten minutes or until all the surfactants are dissolved and the solution is clear. The component D, polyhydric alcohol, if used, is then added slowly with stirring followed by addition of the optional component F, sweetener, preferably previously solubilized in a little water. Colouring agent, hydrogen peroxide (in the form of a 35% aqueous solution), and the remainder of the water are then added in succession.

The pastes and gels may be prepared from the formulation liquids merely by adding the thickener and/or gelling agent and if necessary the peroxygen source to bring it up to specification in the final formula. Alternatively, all of the ingredients are added as above for solution preparation except before adding the peroxide, the gelling agent and or thickener in aliquot portion of water is added followed by the peroxide. In this procedure one may also add the flavours after the thickener rather than at the outset.

EXAMPLES 1 to 6

Mouthrinses are made up having the compositions set out in Table 1 below:

TABLE 1

Example (% w/v)	1	2	3	4	5	6
Ingredient						
Ethanol[1]	4.75	4.75	4.75	4.75	4.75	4.75
Wintergreen Flavour[2]	0.22	0.22	0.22			0.22
Cinnamon Flavour[3]				0.15	0.15	
Pluronic F108	1.0	1.0	1.0	1.0	1.0	1.0
Polysorbate 20[4]	0.6	0.6	0.6	0.6	0.6	0.6
Sorbitol[5]	10.5		10.5	10.5		
Glycerin		5.0			5.0	5.0
Sodium saccharin	0.04	0.04	0.04	0.04	0.04	0.04
FD & C Blue No. 1[6]	.0004	.0004				
FD & C Red No. 40[6]				.002	.002	
Hydrogen peroxide[7]	1.5	1.5	1.5	1.5	1.5	1.5
Purified Water	←qs. to 100 v.→					

Notes on Table 1

[1]In form of 95% soln.
[2]80% Methyl salicylate, 20% menthol.
[3]7.5% Menthol, 35% cinnamic aldehyde, 7.5% clove oil in propylene glycol soln.
[4]Tween 20-polyoxyethylene (20) sorbitan monolaurate.
[5]In form of 70% soln.
[6]In Form of 1% soln.
[7]In form of 35% soln.

All the above-exemplified formulations represent satisfactory, pleasing, acceptable and effective foaming oxygenating mouthrinses having satisfactory storage stability with respect to flavour, colour, appearance, taste, peroxy content and the like.

EXAMPLES 7 to 12

The foregoing Examples 1 to 6 are repeated except 18% of Pluronic F127 gelling agent is provided in

the formulations and in each instance good "ringing" gel is produced. The gelling agent is mixed with a major amount (90%) of the formula water and polyhydric alcohol to which is added the alcohol, flavour and surfactant (F108 and polysorbate) mixture and finally the saccharin, colourant(s) and hydrogen peroxide. The temperature is generally maintained at around 0°C (e.g. −5 to 10°C) during preparation of the water gelling agent mixture and also during addition of other ingredients to this mixture.

EXAMPLE 13

75 Grams of a 70% aqueous solution of sorbitol, 2.0 mg of Blue Dye #1 and 470 ml of water are mixed and cooled to 5°C. To the mixture first there is added 125 grams of Pluronic P127 and after dissolution thereof there are added 1.1 grams of Wintergreen Flavour (as in Example 1 to 6) and 21.4 grams of 35% aqueous hydrogen peroxide (USP). The mixture is allowed to come to room temperature. The next day it is noted that a good gel has formed. The amount of gelling agent (i.e. Pluronic P127) is about 18% by weight.

EXAMPLE 14

Example 13 is repeated except that along with the initial mixture of sorbitol, dye and water there is added 5 grams of Carbopol 934 (a carboxylated vinyl polymer). The resultant product after a few days is a "heavy syrup".

EXAMPLE 15

25 Grams of 95% USP ethanol and 0.85 grams of Wintergreen flavour (0.68 g methyl salicylate and 0.17 g USP menthol) are mixed. To this is added 3.85 g of Pluronic F108 and mixing is done for 20 minutes. Then 1.25 g of water are added with mixing. 2.3 g of Polysorbate 20 N.F. (non-ionic) is added and mixed for 10 minutes. To 2.85 g of water are added 60 g of 70% aqueous sorbitol (USP) and the temperature lowered to 0—5°C. To this cold solution are added 100 g of Pluronic F127. It is noted that temperature drops to −2°C. Mixing is done for 40 minutes. To this cold mixture is added the alcohol, flavour, Pluronic F108, and Polysorbate mixture. Then 0.15 g of sodium saccharin (USP), 0.0015 g FD & C Blue #1, and 21.43 g of 35% aqueous hydrogen peroxide are added and well mixed for about 10 minutes. Excellent gel is formed.

This invention has been disclosed with respect to preferred embodiments, and various modifications and variations thereof obvious to those skilled in the art are to be included within the spirit and purview of this application and the scope of the appended claims.

CLAIMS

1. An aqueous oral composition comprising:
(a) from about 0.5 to about 5% by weight of hydrogen peroxide; and
(b) a flavouring agent selected from the group consisting of:

(1) wintergreen flavour containing methyl salicylate and menthol in a weight ratio of about 3:1 to 5:1; and
(2) cinnamon flavour containing 6—9% menthol, 32—38% cinnamic aldehyde and 6—9% clove oil.

2. An oral composition as claimed in Claim 1 including from about 3 to 10% by weight of ethanol.

3. An oral composition as claimed in Claim 1 or Claim 2 including from about 1 to 20% by weight of polyhydric alcohol.

4. An oral composition as claimed in Claim 1, 2 or 3 including from about 0.1% to about 10% by weight of non-ionic surfactant.

5. An oral composition as claimed in any one of Claims 1 to 4, in which the amount of hydrogen peroxide is from about 1% to about 3%, and which includes about 0.5 to 5% by weight of non-ionic surfactant, about 3—10% by weight of ethanol and about 3—15% by weight of polyhydric alcohol selected from glycerol and sorbitol.

6. An oral composition as claimed in Claim 4 or Claim 5, in which the non-ionic surfactant comprises from about 0.5% to 3% of a water soluble polyoxyethylenated-polyoxypropylene polyol and from about 0.3% to 2% of a water soluble polyoxyethylenated mono-ester of sorbitol with a C_{10} to C_{18} fatty acid.

7. A mouthrinse solution comprising an oral composition as claimed in any one of Claims 1 to 6.

8. An aqueous oral gel comprising an oral composition as claimed in any one of Claims 1 to 6.

9. An aqueous oral gel as claimed in Claim 8 including from about 1% to about 50% of a gelling agent.

10. An aqueous oral gel as claimed in Claim 9, in which the amount of gelling agent is from about 5% to 30% by weight of the gel.

11. An aqueous oral gel as claimed in Claim 9 or Claim 10, in which the gelling agent is a water-soluble carboxymethylcellulose.

12. An aqueous oral gel as claimed in Claim 11, in which the gelling agent is sodium carboxymethyl-cellulose.

13. A mouthrinse as claimed in Claim 7 substantially as specifically described herein with reference to any one of Examples 1 to 6.

14. An aqueous oral gel as claimed in Claim 8 substantially as specifically described herein with reference to any one of Examples 7 to 15.

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